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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire -3- month(s), -0- days from the date of this letter. Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☒ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims ~~1-6, 20, 23+24~~ 1-30 are pending in the application.
   Of the above, claims 7-19, 21, 22 and 25-30 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 1-6, 20, 23+24 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

Part I DETAILED ACTION

Status of Application and Amendments

1. The amendments filed 22 February 1996 have been entered.

~~Claims 7-22 and 25-30 have been cancelled. Claims 1-6, 23 and 24 are under examination.~~

Informalities

2. The disclosure is objected to because of the following informalities: the Brief Description of the Drawings should recite the SEQ ID NO: identifiers for the sequences shown in Figures 2A and 2B. Appropriate correction is required. See MPEP 2422.02

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and / or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And / Or Amino Acid Sequence Disclosures.

1) Each peptide sequence of four or more amino acids must be assigned an identifier and be listed in the Sequence Listing. It appears that the specification contains a number of separate sequences encoding or representing peptides that refer to the sequence in Figure 2A, specifically pages: 15-16, 22, 45, and 53.

2) The required sequence identifier format is SEQ ID NO:. 37 CFR 1.821(c).

Election/Restriction

4. Restriction to one of the following inventions is required under 35 U.S.C. § 121:

Group I. Claims 1-6, 21, 23 and 24, drawn to a protein having the ability to bind the cytoplasmic region of a Fas receptor, purified mammalian protein, a polypeptide fragment, a C-terminal polypeptide fragment having the ability to bind the cytoplasmic region of a Fas receptor, a N-terminal polypeptide fragment having the ability to induce apoptosis, a protein produced by recombinant processes, classified in class 530, subclass 350.

Group II. Claims 7-14, 20 and 22, drawn to a nucleic acid coding for a protein having the ability to bind the cytoplasmic region of a Fas receptor, a nucleic acid that is complementary to the nucleic acids encoding the binding protein and the N-terminal fragment, a composition containing a nucleic acid, a host cell containing a nucleic acid, and a pharmaceutical composition containing a host cell, a process for making a FADD protein, and a process for chemically replicating a nucleic acid molecule, classified in class 435, subclass 69.1.

Group III. Claims 15, 16, and 19, drawn to an antibody capable of forming antibody complex, a nucleic acid encoding a antibody, and a hybridoma cell line classified in class 435 subclass 240, 27.

Group IV. Claims 17 and 18 drawn to an agent having the ability to inhibit binding and a agent that inhibits Fas-associated apoptotic cell death, classified in class 514 subclass 2.

Group V. Claim 21, drawn to a process for chemical synthesizing a FADD protein, classified in class 530, subclass 368.

Group VIa. Claims 25-26, drawn to a method of modulating cellular function by introducing a FADD nucleic acid into a cell, growing a cell and transcribing the FADD protein invivo and ex-vivo, classified in class 514, subclass 44.

Group VIb. Claims 25-26, drawn to a method of modulating cellular function by introducing a FADD nucleic acid into a cell, growing a cell and transcribing the FADD protein invitro, classified in class 935, subclass 60.

Group VII. Claim 27, drawn to a method of modulating cellular function, regulated by Fas receptor pathway by introducing a FADD nucleic acid to a subject, classified in class 514, subclass 44.

Group VIII. Claim 28, drawn to a method of maintaining T cell viability by introducing into the T cell a agent that inhibits Fas-associated apoptotic cell death in vivo and ex-vivo, classified in class 514, subclass 44.

Group IX. Claims 29 and 30, drawn to assay methods of screening for an agent classified in class 435, subclass 7.1.

Group I and Group II are related as associated protein and nucleic acids products. However, the inventions are distinct because: (1) the nucleic acids can be used for materially different purposes other than in the generation of the protein product, such as in the synthesis of probes to detect the presence particular genetic sequences; and (2) the associated protein products can be obtained by other means,

such as biochemical purification using non-recombinant methods, for example. Furthermore, the nucleic acids and protein product are materially, chemically and physically distinct species requiring separate searches.

Group I and III, are related insofar as the proteins claimed as invention I can be used in principle, to generate the antibodies claimed as group III. However, the inventions are distinct because, for example, the antibodies can be used for materially different purposes, such as in a detection assay for the presence of the proteins or as material for effecting purification of these proteins. Furthermore, the products are materially, chemically and physically distinct species requiring separate searches.

Group I and IV are related only insofar as the protein of invention I can be used to identify agents that inhibit FADD protein binding. However, the inventions are distinct because the agents that inhibit FADD protein binding could be used for a materially different purposes such as antibodies for protein purification or molecular weight markers.

Group I and Group V are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (M.P.E.P. § 806.05(f)). In the instant case, the product of Group I is made by a materially different method with steps that are unrelated to the recombinant method of producing the protein.

Group I is not related to any of Groups VI-IX because the product of I is not used in or produced by any process steps in the methods of VI-IX.

Group II and Group III are not related to II and III are directed to materially different compositions of matter having different structures and functions and the products of III are not used in or produced by the method of II.

Group II and IV, V, VIII, IX are disclosed as different combinations which are not connected in design, operation or effect. These combinations are independent if it can be shown that (1) they are not disclosed as capable of use together, (2) they have different modes of operation, (3) they have different functions, or (4) they have different effects. (MPEP 806.04, MPEP 808.01). In the instant case the combinations of FADD nucleic acids are not required to identify FADD inhibitors, treatment, or assay development.

Group II's nucleic acids and the methods of using the product VI and VII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case, the method of using the product VI and VII are alternative materially different processes of using the nucleic acids of Group II.

Group III is not related to V-IX because the antibodies of III are not used in or produced by any process step of V, VI, VII, VIII, or IX.

Groups III and IV are not related and the invention of Group IV is directed to materially different compositions having materially different structures and functions.

Group IV is not related to V-VII because the agent of IV is not used in or produced by any process step in V, VI or VII. Inventions IV an agent and VIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case VIII and IX are alternative materially different processes of using the agent.

The processes of V-IX are unrelated and materially distinct because they are practiced with materially different process steps for materially different purposes.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and because of their recognized divergent subject matter, and because the searches required for the distinct groups are not coextensive, restriction for examination purposes as indicated is proper.

5. During a telephone conversation with Antoinette Konski on 7 June 1996 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-6, 21, 23 and 24. Affirmation of this election must be made by applicant in responding to this Office action. Claims 7- 20, 22, and 25-30 are withdrawn from

further consideration by the Examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

Claim Rejections - 35 USC § 101

6. 35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claim 1 is rejected under 35 U.S.C. § 101 because the claim language does not indicate the hand of man (e.g. a purified protein...or a protein isolated from...,etc.). Hence in their present form these claims encompass products of nature. Claim language incorporating either one of the cited examples above would overcome this rejection.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 20, 23, and 24 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to the fas associated death domain (FADD) proteins identified by SEQ ID NO: 2. See M.P.E.P. §§ 706.03(n) and 706.03(z).

The claims require a FADD polypeptide and polypeptide fragments having the ability to bind the cytoplasmic region of a Fas receptor. Structurally, the claims encompass polypeptides comprising numerous FADD polypeptides and fragments such as, for example, FADD fragments lacking both N-terminal and C-terminal amino acids. Additionally, the claims do not recite which portion(s) of the claimed FADD polypeptides must be present to maintain the ability to bind the cytoplasmic region of a Fas receptor. The disclosure does not teach the repertoire of purified mammalian protein or fragments "having the ability to bind the cytoplasmic region of a Fas receptor". The polypeptides recited in claims 1-6 could be any number of potential polypeptides undisclosed in the specification. The specification does not provide adequate guidance which would enable one skilled in the art to make the ensemble of proteins with the biochemical functions corresponding to those of the instant claims because it does not provide a physical description of each protein capable of corresponding function, i.e. molecular weight and amino acid sequence for each protein.

Claim 1, 2, 4-6, 20, 23 and 24 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

8. Claims 3-5 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to AU1-N-FADD and FADDmt. See M.P.E.P. §§ 706.03(n) and 706.03(z).

Applicants claim a polypeptide fragment of the protein of claim 1. The disclosure does not teach how to make and use the entire ensemble of peptide fragments as claimed, because the cytoplasmic portion of the Fas receptor has binding sites for additional proteins not disclosed in the instant specification, i.e. basophil protein-tyrosine phosphatase binds to the cytoplasmic portion of the receptor, see Maekawa et al. (U). It would be unpredictable to expect the methods provided in the instant application to produce any and all polynucleotides encoding peptides with the ability to bind. Furthermore, it would require undue experimentation to work out the conditions necessary to achieve this result. Two examples were provided, AU1-N-FADD and FADDmt. The specification lacks the guidance needed for a practioner skilled in the art to produce peptide fragments outside of the two aforementioned polypeptides because it does not teach the ensemble of proteins with the corresponding activity.

9. Claim 24 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites "a protein or polypeptide produced by the process of claim 22". The process of claim 22 recites a process for

chemically replicating a nucleic acid and does not include the process steps needed to produce a polypeptide.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1-6, and 20 are rejected 35 U.S.C. § 103 as being unpatentable over Itoh et al.1993 (T) in view of Maekawa et al. 1991 (U), and in further view of Morrison et al. 1989 (V).

Itoh et al. (T) teaches the amino acids of the cytoplasmic region of the Fas antigen responsible for apoptosis known as the *death domain*, see *Signal-transducing Domain in the Fas Antigen* pages 10933-34; and the recombinant production of FADD in a mammalian host cell, see *Cell lines and Transfection*, page 10933. Itoh et al. (T) does not teach a purified mammalian polypeptide or fragment capable of inducing apoptosis. Maekawa et al.(U) teaches the cloning and expression of a protein that

binds to the cytoplasmic region of a Fas antigen known as the human basophil protein-tyrosine phosphatase (PTP-BAS), see figure 1, the *type 1 PTP-BAS isoform*. Maekawa et al.(U) does not teach a purified mammalian protein or fragment capable of inducing apoptosis, and does not teach its recombinant production in a mammalian host cell. Morrison et al. (V) teaches the purification of a protein that binds to the cytoplasmic regions of tyrosine kinase receptors which includes the Fas receptor, see *Immunoprecipitation and Protein Association Assays*, page 656. Morrison et al. (V) does not teach recombinant production of FADD polypeptide. Therefore, it would have been obvious to one having ordinary skill in the art to use the method of Morrison et al. (V) to purify Maekawa et al.'s recombinant protein with the capacity to bind to the cytoplasmic region of a Fas receptor because Maekawa et al.'s protein recognizes a consensus phosphorylation sequence in the carboxy terminus of Fas receptors, see page 10936, second column, Itoh et al. (T). Furthermore, Maekawa et al.'s protein could be expressed in a host cell using the method of Itoh et al. to produce a recombinant protein or fragments that induces apoptosis.

Conclusion

11. The prior art made of record and not specifically relied upon in any rejection cited above is either: (a) considered cumulative to the prior art that was cited in a rejection; (b) considered pertinent to applicant's disclosure and shows the state of the art in its field but is not determined by the Examiner to read upon the invention

currently being prosecuted in this application; or (c) was published after the applicants filing or claimed priority date.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Curtis whose telephone number is (703) 305-6571. The examiner can normally be reached on Monday through Friday from 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stephen Walsh, can be reached on (703) 308-2957. The fax phone number for this Group is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Stephen Walsh
STEPHEN G. WALSH
PRIMARY EXAMINER
GROUP 1800

Joseph Curtis Ph.D
Patent Examiner JC
July 3, 1996